Con Diving

dextran 12,000, carboxylic acid esters of glycerol, sorbitan monostearate, sorbitan monooleate, polyoxamer 188, polyoxamines, alkoxylated ethers, alkoxylated esters, alkoxylated mono-, di and triglycerides, alkoxylated phenols and diphenols, Genapol compounds, Bauki compounds, sodium stearate, metal salts of alcohol sulfates and metal salts of sulfosuccinates and mixtures of two or more of said substances; and

- b) a physiologically acceptable carrier, which allows the transport of said nanoparticles to the target within said mammal after administration.
- 89. (New) The drug targeting system of Claim 88, wherein said nanoparticles comprise particles of said polymeric material having a diameter of less than about 1,000 nm.
- 90. (New) The drug targeting system of Claim 89, wherein said particles have a diameter of between about 1 and up to about 1,000 nm.
- 91. (New) The drug targeting system of Claim 88, wherein said polymeric material is selected from the group consisting of polyacrylates, polymethacrylates, polyacrylates, polyacrylates,
- 92. (New) The drug fargeting system of Claim 88, wherein said one or more physiologically effective substances are adsorbed, absorbed or incorporated into said nanoparticles or a combination thereof.
- 93. (New) The drug targeting system of Claim 88, wherein said one or more physiologically effective substances comprise a therapeutic substance and a diagnostic substance.
- 94. (New) The drug targeting system of Claim 88, wherein said one or more physiologically effective substances comprise a substance which has central nervous system

activity but cannot cross the blood brain barrier without modification or without a carrier.

95. (New) The drug targeting system of Claim 93, wherein said therapeutic agent is selected from the group consisting bf drugs acting at synaptic sites and neuroeffector junctional sites; general and local analgesics; hypnotics and sedatives; drugs for the treatment of psychiatric disorders; antiepileptics and anticonvulsants; drugs for the treatment of Parkinson's and Huntington's disease, aging and Alzheimer's disease; excitatory amino acid antagonists, neurotrophic factors and neuroregenerative agents; trophic factors; drugs for the treatment of CNS trauma or stroke; drugs for the treatment of addiction and drug abuse; antacoids and anti-inflammatory drugs; chemotherapeutic agents for parasitic infections and diseases caused by microbes; immunosuppressive agents and anti-cancer drugs; hormones and hormone antagonists; heavy metals and heavy metal antagonists; antagonists for nonmetallic toxic agents; cytostatic agents for the treatment of cancer; diagnostic substances for use in nuclear medicine; immunoactive and immunoreactive agents; transporter inhibitors; antibiotics; antispasmodics, antihistamines; antinauseants; relaxants; stimulants; sense and antisense oligonucleotides; rerebral dilators; psychotropics; antimanics; vascular dilators and constrictors; anti-hypertensives; drugs for migraine treatment; hypnotics, hyperglycemic and hypoglycemic agents; miherals and nutritional agents; anti-obesity drugs; anti-asthmatics; and mixtures thereof.

- 96. (New) The drug targeting system of Claim 95, wherein said psychiatric disorders comprise depression or schizophrenia or both.
- 97. (New) The drug targeting system of Claim 93, wherein said diagnostic substance is selected from the group consisting of substances for nuclear medicine and radiation therapy.
  - 98. (New) The drug targeting system of Claim 88, wherein said one or more

stabilizers comprise a substance selected from the group consisting of polysorbate 85 and dextran 12,000 and mixtures thereof and mixtures of said stabilizers with other stabilizers.

99. (New) The drug targeting system of Claim 88, wherein said carrier is selected from the group consisting of water, physiologically acceptable aqueous solutions containing salts or buffers, or a mixture thereof, and any other solution acceptable for administration to a mammal.

100. (New) The drug targeting system of Claim 88, wherein said one or more stabilizers allow release of said one or more physiologically active substances from said nanoparticles and passage of said one or more physiologically active substances through a blood brain barrier of said mammal separate from said nanoparticles.

101. (New) A method for preparing a drug targeting system for administering one or more physiologically effective substances to a mammal, said method comprising:

a) preparing nanoparticles made of a polymeric material, said nanoparticles being free of a surfactant surface coating and comprising said polymeric material, one or more physiologically effective substances to be delivered to said mammal, and one or more stabilizers for said nanoparticles allowing targeting of said one or more physiologically effective substances to a specific site within or on a mammalian body, said one or more stabilizers being selected from the group consisting of polysorbate 85, polysorbate 81, dextran 12,000, carboxylic acid esters of glycerol, sorbitan monostearate, sorbitan monooleate, polyoxamer 188, polyoxamines, alkoxylated others, alkoxylated esters, alkoxylated mono-, di and triglycerides, alkoxylated phenols and diphenols, Genapol compounds, Bauki compounds, sodium stearate, metal salts of alcohol sulfates and metal salts of sulfosuccinates and mixtures of two or more of said substances; by polymerizing one or more monomeric or oligomeric precursors of said polymeric material or both, in the

202 E3 tras presence of said one or more physiologically effective substances and in the presence of said stabilizers; and optionally

b) providing said nanoparticles in a medium allowing the transport of said nanoparticles to a target within or on said mammal after administration.

102. (New) A method for preparing a drug targeting system for administering one or more physiologically effective substances to a mammal, said method comprising:

- a) preparing nanoparticles made of a polymeric material, said nanoparticles being free of a surfactant surface coating and comprising said polymeric material and one or more stabilizers for said nanoparticles, said one or more stabilizers being selected from the group consisting of polysorbate 85, polysorbate 81, dextran 12,000, carboxylic acid esters of glycerol, sorbitan monostearate, sorbitan monooleate, polyoxamer 188, polyoxamines, alkoxylated ethers, alkoxylated esters, alkoxylated mono, di and triglycerides, alkoxylated phenoles and diphenoles, Genapo compounds, Bauki compounds, sodium stearate, metal salts of alcohol sulfates and metal salts of sulfosuccinates and mixtures of two or more of said substances; by polymerizing one or more monomeric or oligomeric precursors of said polymeric material or both, in the presence of said stabilizers;
- b) loading one or more physiologically effective substances to be delivered to said mammal into or onto said nanoparticles or both; and optionally
- c) providing said loaded nanoparticles in a medium allowing the transport of said nanoparticles to the target within or on said mammal after administration.
- 103. (New) The method of Claim 101, wherein said polymerization step is selected from the group consisting of emulsion polymerization, interfacial polymerization, solvent deposition, solvent evaporation and crosslinking oligomers or polymers or both, in solution.

104. (New) The method according to Claim 101, wherein, in the polymerization

step, a polymeric material is formed which is selected from the group consisting of polyacrylates, polymethacrylates, polycyanoacrylates, polyarylamides, polylactates, polyglycolates, polyanhydrates, polyorthoesters, gelatin, polysaccharides, albumin, polystyrenes, polyvinyls, polyacrolein, polyglutaraldehydes and copolymers and mixtures thereof.

J.

' 105. (New) The method of Claim 101, wherein said loading step comprises mixing said nanoparticles with a solution of said one or more physiologically effective substances and allowing a sufficient time for an effective amount of said one or more physiologically effective substances to be adsorbed onto or absorbed by said nanoparticles or both.

(New) The method of Claim 102, wherein said polymerization step is selected from the group consisting of emulsion polymerization, interfacial polymerization, solvent deposition, solvent evaporation and crosslinking oligomers or polymers or both, in solution.

107. (New) The method of Claim 102, wherein, in the polymerization step, a polymeric material is formed which is selected from the group consisting of polyacrylates, polymethacrylates, polycyanoacrylates, polyarylamides, polylactates, polyglycolates, polyanhydrates, polyorthoesters, gelatin, polysaccharides, albumin, polystyrenes, polyvinyls, polyacrolein, polyglutaraldehydes and copolymers and mixtures thereof.

108. (New) The method of Claim 102, wherein said loading step comprises mixing said nanoparticles with a solution of said one or more physiologically effective substances and allowing a sufficient time for an effective amount of said one or more physiologically effective substances to be adsorbed onto or absorbed by said nanoparticles or both.

109. (New) The method of Claim 101, wherein said one or more stabilizers are selected from the group consisting of polysorbate 85 and dextran 12,000 and mixtures thereof and mixtures of said stabilizers with other stabilizers.

(New) The method of Claim 102, wherein said one or more stabilizers are selected from the group consisting of polysorbate 85 and dextran 12,000 and mixtures thereof and mixtures of said stabilizers with other stabilizers.

the (New) The method of Claim 101, wherein said one or more physiologically effective substances are selected from the group consisting of a therapeutic substance and a diagnostic substance.

112. (New) The method of Claim 102, wherein said one or more physiologically effective substances are selected from the group consisting of a therapeutic substance and a diagnostic substance.

113. (New) The method of Claim 191, wherein said one or more physiologically effective substances have central nervous system activity but cannot cross the blood brain barrier without modification or without a carrier.

(New) The method of Claim T02, wherein said one or more physiologically effective substances have central nervous system activity but cannot cross the blood brain barrier without modification or without a carrier.

active substances are selected from the group consisting of drugs acting at synaptic sites and neuroeffector junctional sites; general and local analgesics; hypnotics and sedatives; drugs for the treatment of psychiatric disorders; anti-epileptics and anticonvulsants; drugs for the treatment of Parkinson's and Huntington's disease, aging and Alzheimer's disease; excitatory amino acid antagonists, neurotrophic factors and neuroregenerative agents; trophic factors; drugs aimed at the treatment of CNS trauma or stroke; drugs for the treatment of addiction and drug abuse; antacoids and anti-inflammatory drugs; chemotherapeutic agents for parasitic infections and diseases caused by microbes; immunosuppressive agents and anti-

-7-

cancer drugs; hormones and hormone antagonists; heavy metals and heavy metal antagonists; antagonists for non-metallic toxic agents; cytostatic agents for the treatment of cancer; diagnostic substances for use in nuclear medicine; immunoactive and immunoreactive agents; transporter inhibitors; antibiotics; antispasmodics; antihistamines; antinauseants; relaxants; stimulants; sense and antisense oligonucleotides; cerebral dilators; psychotropics; antimanics; vascular dilators and constrictors; anti-hypertensives; drugs for migraine treatment; hypnotics, hyperglycemic and hypoglycemic agents; minerals and nutritional agents; anti-obesity drugs; anti-asthmatics; and mixtures thereof.

19 15 (New) The method of Claim N.5, wherein said psychiatric disorders comprise depression and schizophrenia.

(New) The method of Claim 102, wherein said one or more physiologically active substances are selected from the group consisting of drugs acting at synaptic sites and neuroeffector junctional sites; general and local analgesics; hypnotics and sedatives; drugs for the treatment of psychiatric disorders; anti-epileptics and anticonvulsants; drugs for the treatment of Parkinson's and Huntington's disease, aging and Alzheimer's disease; excitatory amino acid antagonists, neurotrophic factors and neuroregenerative agents; trophic factors; drugs aimed at the treatment of CNS trauma or stroke; drugs for the treatment of addiction and drug abuse; antacoids and anti-inflammatory drugs; chemotherapeutic agents for parasitic infections and diseases caused by microbes; immunosuppressive agents and anticancer drugs; hormones and hormone antagonists; heavy metals and heavy metal antagonists; antagonists for non-metallic toxic agents; cytostatic agents for the treatment of cancer; diagnostic substances for use in nuclear medicine; immunoactive and immunoreactive agents; transporter inhibitors; antibiotics; antispasmodics; antihistamines; antinauseants; relaxants; stimulants; sense and antisense oligonucleotides; cerebral dilators; psychotropics; antimanics;

vascular dilators and constrictors; anti-hypertensives; drugs for migraine treatment; hypnotics, hyperglycemic and hypoglycemic agents; minerals and nutritional agents; anti-obesity drugs; anti-asthmatics; and mixtures thereof.

18. (New) The method of Claim 117, wherein said psychiatric disorders comprise depression and schizophrenia.

(New) The method of Claim 191, wherein said diagnostic substance is selected from the group consisting of substances for nuclear medicine and radiation therapy.

120. (New) The method of Claim 102, wherein said diagnostic substance is selected from the group consisting of substances for nuclear medicine and radiation therapy.

(New) The method of Claim 101, wherein said medium allowing the transport of said nanoparticles to the target within said mammal after administration is selected from the group consisting of water, physiologically acceptable aqueous solutions containing salts or buffers or a mixture thereof, and any other solution acceptable for administration to a mammal.

123. (New) The method of Claim 162, wherein said medium allowing the transport of said nanoparticles to the target within said mammal after administration is selected from the group consisting of water, physiologically acceptable aqueous solutions containing salts or buffers or a mixture thereof, and any other solution acceptable for administration to a mammal.

- 123. (New) A method of targeting one or more physiologically effective substances to a specific target within or on a mammalian body, which comprises administering the drug targeting system of Claim 88, to a mammal.
- 124. (New) The method of plaim 123, wherein said administered drug targeting system effects passage of said one of more physiologically effective substances through a

blood brain barrier of said mammal.

125. (New) The method of Claim 123, wherein said mammal is a human.

126. (New) The method of Claim 127, wherein said administration is effected by an oral, intravenous, subcutaneous, intramuseurar, intranasal, pulmonal or rectal route.

- 127. (New) The method of Claim 126, wherein said administration is effected by an oral or intravenous route.
- 128. (New) The method of Claim 126, wherein said targeting comprises crossing a blood-brain barrier of said mammal.
- 129. (New) The method of Claim 126, wherein said one or more physiologically effective substances effect a central nervous system of said mammal.
- 130. (New) The method of Claim 126, which effects a pharmacological effect on a central nervous system of said mammal, wherein said one or more physiologically active substances do not otherwise pass a blood-brain barrier of said mammal.
- 131. (New) The drug delivery system of Claim 88, wherein said nanoparticles are made of polybutylcyanoacrylate.
- (New) The method of Claim 101, wherein said nanoparticles are made of polybutyleyanoacrylate.
- (New) The method of Claim 102, wherein said nanoparticles are made of polybutylcyanoacrylate.
- 134. (New) The method of Claim 126, wherein said nanoparticles are made of polybutylcyanoacrylate.

## **REMARKS**

Claims 41-87 have been canceled. New Claims 88-134 have been added and are now